



True Congenital Cysts of the Pancreas in the Newborn and Infant

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Abstract

Objectives: True congenital pancreatic cysts (CPC) are extremely rare, only 27 cysts were reported so far in children under 3 years of age. With several new cases reported here, conclusions for diagnostic work up and treatment can be drawn.

Material and Methods: 4 cases with CPC are analyzed retrospectively and reviewed together with all previously published cases.

Results: Girls were affected by CPC about twice as frequent as boys, cysts were localized more often in the tail than in the head or body of the pancreas. Unilocular cysts are seen more frequent than multilocular cysts. Diagnosis can be made by prenatal or postnatal ultrasound. Usually, total excision of the cyst(s) was performed and prognosis was good in otherwise healthy children.

Conclusion: This rare diagnosis should be considered when cystic lesions appear in routine antenatal ultrasound. The benign nature of these cysts together with a certain risk for complications when left in place justifies for a planned surgical approach in the neonate aiming at total excision of the cyst with preservation of the pancreas. Ultrasound is sufficient for preoperative imaging.

Keywords: Pancreatic cyst; Congenital; Prenatal diagnosis; Pediatric

Introduction

The rareness of true CPC and the fact that it is increasingly detected nowadays by prenatal ultrasound rather than by gastrointestinal symptoms in the adult requires an update on this disorder for the obstetrician, pediatric surgeon and pediatric gastroenterologist. True pancreatic cysts may be congenital or of neoplastic [1,2] or hydatid [3] origin. An epithelial lining of the luminal surface and a lack of inflammatory cells are diagnostic for true CPC which is extremely rare, previously reported in 27 infants (0-3 years). A first description and first successful operation of a congenital developmental pancreatic cyst in an infant dates back to 1895 [4]. In 1959, Miles [5] reviewed 8 cases in infancy, 2 of these however showed no epithelial lining in pathology [Eha, McPherson] and are therefore eliminated from review. Thereafter, 24 live born cases were reported [6-33].

Only 12 of these had a prenatal diagnosis [12,14-18,20-22,24,27,31] made at 21 weeks [27], 24 weeks [21], 26 weeks [31], 27 weeks [17,22], 30 weeks [14,26], 32 weeks [15,16], 33 weeks [24] and 36 weeks [18] of gestation.

Solitary cysts were found to have a good prognosis in contrast to polycystic pancreatic malformation [34] which may be associated with cystic malformation of other organs. Cystic fibrosis, Beckwith-Wiedemann syndrome. [18,35] and Hoppel-Lindau disease [11] may be present in patients affected with polycystic pancreas. A syndrome related occurrence of CPC was suspected in Ivemark II syndrome [30].

A retrospective analysis of cases of CPC treated in two German university pediatric surgery departments (Mainz and Tübingen) over a period of 20 years was made. Four cases of congenital pancreatic cysts (cases 1-3: Tübingen, case 4: Mainz) with differences in clinical presentation and diagnostic evaluation were found and are reported in the following. All previously reported congenital pancreatic cysts in children were reviewed to give an overview of this entity.

Case Presentation 1

A 2 years and 7 month old girl presented with partially bilious vomiting for 10 days and a weight reduction of 450 g. Nocturnal and postprandial abdominal pain was complained of Blood

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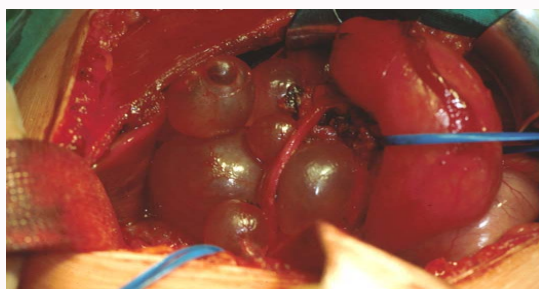


Figure 1, Case 2: Intraoperative aspect of polycystic tumor of the pancreatic head with retroduodenal extension, visible after duodenal mobilisation.

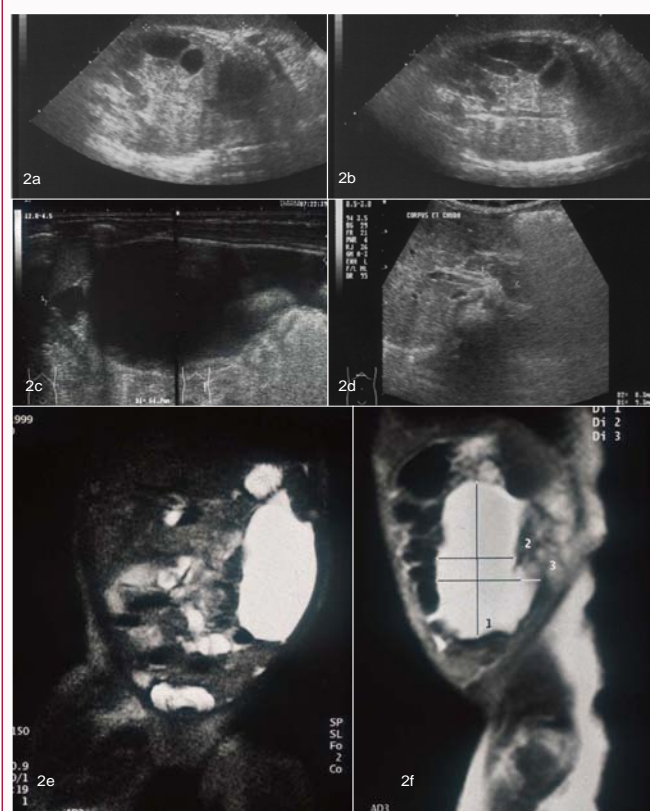


Figure 2a-f, Case 4: 2 a + b: Prenatal ultrasound performed at 33⁺³ (Figure 2a) and 35⁺⁴ weeks (Figure 2b) of gestation, demonstrating rapid growth of the cystic intra-abdominal lesion (orientation of fetus: caudal left, cranial right, ventral upside).

2c: Preoperative ultrasound of left abdomen at age 11 days. A small cranial and a large caudal cyst extend over the entire left half of the abdomen. The small cyst is close to the pancreas.

2d: Postoperative ultrasound at age 7 months. Cross section of the epigastrium, showing regular size and texture of the pancreatic body and tail.

2e+f: Preoperative MRI scans of the abdomen at age 6 days. Frontal (Figure 2e) and sagittal plane (Figure 2f). Similar finding as in preoperative ultrasound with small cranial and large caudal cystic lesion.

chemistry was normal. A plain abdominal x-ray showed a duodenal distension with little intraluminal gas beyond the ligament of Treitz. Ultrasound revealed a 3 x 2.5 cm cyst in the body of the pancreas. Intraoperatively, a solitary cyst arising with a vascularized hilus from the body of the pancreas was found. The cyst was resected; it contained proteinaceous fluid that was lipase (80 U/L) and amylase (82 U/L) positive. Histology of the cyst wall showed pancreatic tissue with acini but without Langerhans islets, the luminal surface of cyst was covered by flat epithelium. The postoperative course was uneventful, a control

ultrasound at 6 months after the operation was normal.

Case Presentation 2

An 8 months old boy, normally developed, was referred because of bilious vomiting and food neglect in the past two weeks. A mandarin-sized painful tumor was palpable in the epigastrium. Serum bilirubin (1.8 mg/dL) and serum amylase (120 U/L) were elevated, other blood parameters (lipase, liver enzymes) were within normal range. Ultrasound showed a cystic tumor to the right of the duodenum and a choledochocoele was suspected. A multicystic tumor of the head of the pancreas with retroduodenal extension was found intraoperatively (Figure 1). A single tubular connection to the main pancreatic duct was isolated and dissected. The cysts were excised, a resection of the pancreatic head was not performed. Histology showed either thick fibrous or membranous cyst wall partially with typical pancreatic tissue containing acini but no Langerhans islets. The luminal surface was covered by flat cuboidal epithelium. Some spots with few inflammatory cells (lymphocytes, macrocytes) were detected. 6 months postoperatively the child was free of symptoms of pancreatitis or cholestasis, blood chemistry and ultrasound were normal.

Case Presentation 3

A cystic tumor (2 x 2 cm) in the upper left abdomen of a male fetus (32 weeks of gestation) was detected by routine ultrasound. After uncomplicated delivery this finding was confirmed by ultrasound. Blood parameters of the child were normal and the child developed normal for 5 month under close observation. When the child began to vomit increasingly and tolerated less food, the cyst that meanwhile had grown to 3 x 2 cm was operated. A solitary retroduodenal cyst with a hilus to the head of the pancreas was found and resected. The hilus of the cyst contained blood vessels and a narrow duct. The cyst fluid was amylase (15 U/L) and lipase (21 U/L) positive. Histologically, a thin membranous cyst wall was seen with acinar structures and some deformed Langerhans islets. The inner surface was partly covered by flat cuboidal epithelium and partly consisted of connective tissue without epithelium. Besides single lymphocytes, no inflammatory cells were detected. A follow-up ultrasound at 6 month postoperatively was normal.

Case Presentation 4

In a female fetus of 30 wk gestation, a cystic tumor in the abdomen was diagnosed upon a routine screening ultrasound (Figure 2a,b). The child was born by vaginal delivery at 37 weeks of gestation with a weight of 3000 g. The early postnatal period was uneventful and the child was referred for surgical treatment on day 6 on a full oral diet and without any abdominal symptoms or irregular laboratory parameters.

Postnatal ultrasound (Figure 2c) confirmed the MRI finding (Figure 2e,f) of a 5 x 6 x 4 cm cystic tumor in the left side of the abdomen. Bilirubin, alcalic phosphatase, liver enzymes, serum amylase and lipase were within normal range. Preoperative differential diagnosis included intestinal duplication, a mesenteric cyst, and ovarian cyst, splenic and pancreatic cyst.

Surgery was performed at the age of 9 days. Intraoperatively, a large cyst was seen in the left abdomen. Adhesions to the lateral abdominal wall, the left colonic flexure, the omentum majus, and splenic hilus were dissected easily. A tight adhesion of the cyst to the tail of the pancreas was then seen (Figure 3a). This pedicle-like

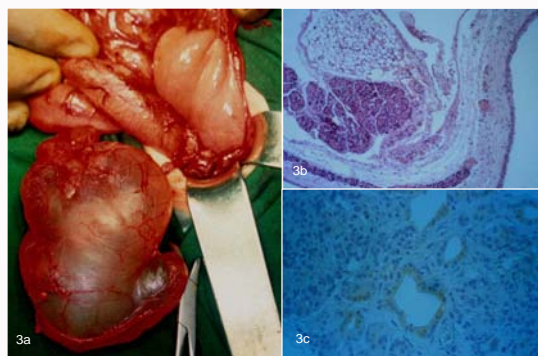


Figure 3a-c, Case 4: 3a: Intraoperative view of the eventrated cyst with its pedicle to the pancreatic tail. Adhesions to the splenic vessels, colon and abdominal wall were removed. 3b: Pathology specimen of the completely resected cyst. 3c: Microphotograph of cyst wall with Langerhans' islets, acinar structures and epithelial lining.

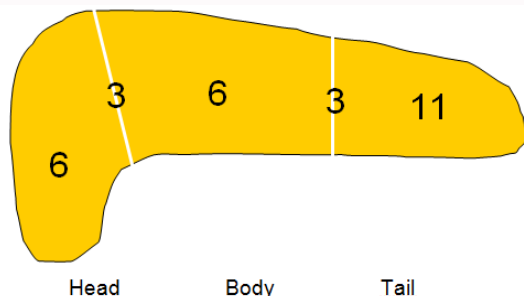


Figure 4: Localisation of congenital pancreatic cysts in 29 cases with known localisation. Cysts were found to arise more frequently from the tail than from the head or body of the pancreas.

structure contained the blood vessels supplying the cyst. The hilus of the cyst was ligated, dissected and the entire cyst and the pedicle were removed. The remaining pancreas was macroscopically free of cysts.

Histology of this tissue showed parts of exocrine pancreatic tissue and fibrous tissue containing a vascular pedicle. Histology of the cyst wall showed a PAS-positive epithelial lining and islets of glandular tissue with ductal ectasia (Figure 3b,c). The epithelial lining of these ducts was slightly reactive to antibodies against pancreatic amylase. The liquid content of the cyst was sterile, free of hemoglobin, and contained lipase (130 U/l), amylase (3 U/l) and protein (1 g/l). The corresponding serum concentrations were within normal range (lipase 19 U/l, amylase <100 U/l, protein 62 g/l).

The postoperative course was uneventful, a complete recovery was made. Upon the last follow up at 8 months after the operation, no residual or recurrence was found. Control ultrasound studies were without pathologic findings (Figure 2d).

Discussion

Pathogenesis

Ectasia of pancreatic ducts has been accused as the major reason for the formation of intraparenchymal pancreatic cysts. Since the pancreas exhibits exocrine function already in early fetal life, pancreatic cysts may appear on ultrasound before 30 weeks of gestation. Pancreatic pseudocysts may be congenital as well but are no true cysts since an epithelial lining is missing.

Diagnostic procedures

Pancreatic cysts are a rare cause of a fetal intraabdominal mass [5], only in recent decades prenatally detectable by ultrasound [17]. Before the era of prenatal high-resolution sonography most congenital pancreatic cysts were diagnosed at higher age, usually when an abdominal mass became palpable or when gastrointestinal symptoms occurred due to compression of adjacent viscera [36] during childhood [37], adolescence, or in adult patients [13].

The currently reported cysts were diagnosed at 30 and 32 weeks of gestation (cases 3,4) or postnatally at 8 and 19 months of age (cases 1,2). Since considerable postnatal growth of congenital pancreatic cysts has been reported [17], prenatal diagnosis and early operation may avoid complications due to extrinsic pressure on adjacent organs as seen in cases 1-3 and in some cases in literature [7,19,32,38]. An increasing number of prenatally detected pancreatic cysts may be expected along with the rapid spread of routine prenatal ultrasound. However, prenatal ultrasound cannot differentiate between pancreatic cysts and pancreatic pseudocysts, which may also be visible before birth [39].

For preoperative diagnostic work up, plain abdominal radiograms, barium x-ray studies, angiography [9], sonography [17], CT scan [12] and MRI [25,27] were employed so far. Postnatal MRI scans were reported only occasionally in this condition. For preoperative topographic evaluation, however, sonography offers sufficient information with a spatial resolution exceeding that of an MRI scan in the neonate (for direct comparisons see Figure 2c and 2e). This is confirmed by the other reports of MRI-findings in this entity, made in 3 days [27], 4 months [25] and 15 months [32] old infants. Ultrasound may therefore be regarded as the gold standard in the diagnosis of cystic intraabdominal tumors in the neonate.

Important features of congenital pancreatic cysts

Including the present cases, antenatal diagnosis was made in 14 of 25 children so far since the first description of antenatal diagnosis by Hopper in 1979. If the diagnosis is not made antenatally, it is usually delayed for some months, with an average age at diagnosis (among 11 children of 0-3 years after 1979) of 8.7 months. Among all children younger than 3 years were 10 boys and 23 girls, the sex was not indicated in 2. The sex ratio is therefore 1:2.3 with a female predominance [40]. The localization of the cyst was not specified in 5 cases. In 11 cases the cyst arose from the tail, in 3 cases from tail and body, in 6 from the body, in 3 from body and head, and in 6 cases from the head of the pancreas. The tail of the pancreas is thus involved more frequently than the head or body of the pancreas (Figure 4). Unilocular cysts (n=24) were seen more frequent than multilocular cysts (n=8) [12].

The content of pancreatic enzymes of the cyst fluid was described only in 20 of the cases. A low enzyme concentration was reported in 8, a high concentration in 6 patients. In 4 cases, no pancreatic enzymes were detected in the cyst fluid and no data were given in 15 cases.

After 1920, mortality from pancreatic cysts was 0% among published cases, excluding cases with severe associated malformations where mortality was high (4 of 5 patients). In otherwise healthy children, pancreatic cysts thus have an excellent prognosis.

Treatment

Since total resection is the treatment of choice in pancreatic cysts whenever feasible, all of the currently reported cases were treated by

Table 1: Literature overview of congenital true pancreatic cysts in neonates and infants. Cases of children older than 3 years upon diagnosis, numerous cases with manifestation in adulthood and cases of stillborn children with pancreatic cysts are not included. Cysts of heterotrophic pancreatic tissue are not included as well.

Author	year	diagn	sex	origin	locula	lining	enzyme	therapy	syndr	surv
Richardson [4]	1895	13 mo	?	T	?	Epith	?	Excision	?	Yes
Railton [44]	1896	6 mo	F	T	Uni	?	?	Drainage	?	No
Telling [45]	1909	11 mo	F	H	Uni	Epith	No	Drainage	No	Yes
Connolly [46]	1911	10 mo	F	H	Uni	?	No	None	?	No
Friedenwald [47]	1926	16 mo	M	?	?	?	No	Drainage	?	Yes
DeLange [48]	1948	6 wk	F	?	Uni	Epith	Yes	None	Yes	No
Miles [5]	1959	1 wk	F	H/B	Multi	Epith	Low	Excision	No	Yes
Power [6]	1961	3 wk	M	B?	Uni	Epith	Low	Marsup.	No	Yes
Siafarikas [8]	1971	5 mo	F	B/T	Multi	Epith	?	Excision	No	Yes
Mares [9]	1977	20 mo	F	B	Multi	Epith	High	Drainage	No	Yes
Hopper [15]	1979	prenat	F	H?	?	?	?	None	Yes	No
Baker [17]	1990	prenat	F	T	Multi	Epith	?	Excision	No	Yes
Fleet [16]	1992	prenat	M	B/T	Uni	Epith	?	Ex/Drain	No	Yes
Auringer [12]	1993	4 mo	F	T	Multi	Epith	?	Excision	No	Yes
Daher [14]	1996	prenat	F	T	Uni	Epith	Low	Excision	No	Yes
Fremond [18]	1997	prenat	M	H	Uni	Epith	Low	Drainage	Yes	No
Maiullari [20]	2000	15 mo	F	B/T	Uni	Epith	High	Excision	No	Yes
Kebapci [21]	2000	prenat	F	T	Uni	Epith	No	Excision	No	Yes
Sepulveda [22]	2000	prenat	M	?	Multi	?	?	Excision	Yes	Yes
Liao [24]	2003	prenat	F	T	Uni	Epith	?	Excision	No	Yes
Kazez [25]	2006	4 mo	M	T	Uni	Epith	Low	Excision	No	Yes
Matta	2006	4 mo	F	H/B	Uni	Epith	High	Drainage	No	Yes
Choi [26]	2007	prenat	F	T	Uni	Epith	Low	Excision	No	Yes
Chung [27]	2007	prenat	F	?	Uni	Epith	?	Excision	No	Yes
Ishimaru [28]	2009	6 mo	M	B	Uni	Epith	High	Excision*	No	Yes
Castellani [29]	2009	prenat	F	B	Uni	Epith	High	Drainage*	No	Yes
Chahed [30]	2012	2 wk	M	?	Uni	?	?	Drainage	Yes	No
Gerscovitch [31]	2012	prenat	?	T	Multi	Epith	?	Excision	No	Yes
Al-Salem [32]	2014	18 mo	M	B	Uni	Epith	?	Excision	No	Yes
Al-Salem [32]	2014	4 mo	F	H/B	Uni	Epith	High	Drainage	No	Yes
Warnock [33]	2016	5 wk	F	?	Uni	?	?	Excision*	No	Yes
Berger	2016	31 mo	F	B	Uni	Epith	Low	Excision	No	Yes
Berger	2016	8 mo	M	H	Multi	Epith	?	Excision	No	Yes
Berger	2016	prenat	F	H	Uni	Epith	Low	Excision	No	Yes
Berger	2016	prenat	F	T	Uni	Epith	Low	Excision	No	Yes

Abbreviations: Age= wk= weeks; mo= Months; Diagn= Age at Diagnosis; Prenat= prenatally; y= Years

Sex: F= Female; M= Male;

Origin: H= Head; B= Body; T= Tail

Locula= Locularity: Uni= Unilocular; Multi= Multilocular; Bi= Bilocular

Lining: Epith= Epithelium; Syndr= Associated Malformations; Surv= Survival

*= Recurrence

complete excision. An exception to this rule should only be made when major damage to the pancreas has to be expected as in large cysts of the pancreatic head. Those conditions should then better be treated by drainage of the cyst into the duodenum or to a jejunal loop by a Roux-en-Y procedure (11 cases). In literature however, most cysts were excised. Treatment by excision (laparotomy) was successful in all 19 cases where it was employed. Recurrence of a cyst has only been reported so far in 2 of 2 cases after laparoscopic resection [33].

Conclusion

It is concluded that CPC will be diagnosed increasingly by routine prenatal ultrasound thus avoiding complications that were seen previously when such cysts were only diagnosed secondary to growth induced compression of adjacent organs. It is assumed from several reported cases [41-43] that cystic intraabdominal tumors may also arise from ectopic pancreatic tissue and show similar histologic features and cyst fluid composition as pancreatic cysts of

the pancreas itself. Analysis of the current cases and the findings in literature revealed a female predominance, preferred localization in the pancreatic tail, cuboid epithelial lining of the lumen, and usually low pancreatic enzyme concentration of congenital pancreatic cysts. Early sonographic diagnosis (prenatal diagnosis in 2/3 of cases) of cyst affecting the body and tail of the pancreas should be followed by total excision which yields an excellent prognosis. Results of the first cases of excision by laparoscopy are not satisfying until now. Cysts originating from the pancreatic head sometimes require internal drainage if excision is not feasible.

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